

IN THE CLAIMS:

This listing replaces all prior claims.

Claim 1. (Original) A method for delaying or reversing a retinal or choroidal degenerative disease or condition in a subject, the method comprising contacting a retinal or choroidal cell of a subject having, or at risk of developing, a retinal or choroidal degenerative disease or condition with an agent that modulates the expression or activity of an AMDP-related or phagocytosis-related gene.

Claim 2. (Original) The method of claim 1, wherein said AMDP-related or phagocytosis-related gene is selected from the group consisting of human unknown PHG-1; prostaglandin D2 synthase; myelin basic protein; human unknown PHG-4; human unknown PHG-5; human peanut-like 2/septin 4; coactosin-like 1; clusterin; casein kinase 1 epsilon; ferritin heavy polypeptide 1; metargidin; human unknown PHG-13; retinaldehyde binding protein 1; actin gamma 1; matrix metalloproteinase, membrane-associated 1 (MT1-MMP); SWI/SNF related/OSA-1 nuclear protein; and human unknown AMDP-3; said AMDP-related or phagocytosis-related genes comprising the respective nucleotide sequences identified as SEQ ID NOS:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, and 17.

Claim 3. (Original) The method of claim 2, wherein said AMDP-related or phagocytosis-related gene is matrix metalloproteinase, membrane-associated 1 (MT1-MMP), said gene comprising the nucleotide sequence of SEQ ID NO:15.

Claim 4. (Original) The method of claim 1, wherein said retinal or choroidal degenerative disease or condition is age-related macular degeneration (AMD).

Claim 5. (Original) The method of claim 4, wherein said subject suffers from AMD.

Claim 6. (Original) The method of claim 4, wherein said subject is at risk of developing AMD.

Claim 7. (Original) The method of claim 1, wherein the method delays the retinal or choroidal degenerative disease or condition.

Claim 8. (Original) The method of claim 1, wherein the method reverses the retinal or choroidal degenerative disease or condition.

Claim 9. (Original) The method of claim 1, wherein said cell is a photoreceptor, an RPE cell, a Muller cell, or a cell type of the choroid selected from the group consisting of an endothelial cell, a smooth muscle cell, a leukocyte, a macrophage, a melanocyte and a fibroblast.

Claim 10. (Original) The method of claim 9, wherein said AMDP-related or phagocytosis-related gene is MT1-MMP, and said MT1-MMP is located within said cell.

Claim 11. (Original) The method of claim 9, wherein said AMDP-related or phagocytosis-related gene is MT1-MMP and said MT1-MMP is located in an extracellular matrix.

Claim 12. (Original) The method of claim 11, wherein said extracellular matrix is an interphotoreceptor matrix.

Claim 13. (Original) The method of claim 1, wherein said agent down-regulates expression of a nucleic acid or amino acid sequence of an AMDP-related or phagocytosis-related gene, said gene selected from the group consisting of MT1-MMP, prostaglandin D2 synthase and AMDP-3.

Claim 14. (Original) The method of claim 13, wherein said agent is an oligonucleotide selected from the group consisting of a ribozyme, an antisense RNA, an interfering RNA (RNAi) molecule and a triple helix forming molecule.

Claim 15. (Original) The method of claim 13, wherein said agent is an antibody that specifically binds to a MT1-MMP, prostaglandin D2 synthase or AMDP-3 protein or peptide.

Claim 16. (Original) The method of claim 15, wherein said antibody neutralizes at least one biological activity of MT1-MMP, prostaglandin D2 synthase or AMDP-3.

Claim 17. (Original) The method of claim 16, wherein said AMDP-related or phagocytosis-related gene is MT1-MMP and said biological activity is activation of progelatinase A or degradation of extracellular matrix.

Claim 18. (Original) The method of claim 13, wherein said agent is a small molecule.

Claim 19. (Original) A method of determining risk of a subject of developing a retinal or choroidal degenerative disease or condition, the method comprising screening a nucleic acid sequence of said subject for the presence of at least one polymorphism in at least one phagocytosis-related or AMDP-related gene, wherein the presence of a polymorphism in at least one of said genes indicates that the subject is at higher risk for developing a a retinal or choroidal degenerative disease or condition, than a subject without said polymorphism.

Claim 20. (Original) The method of claim 19, wherein said phagocytosis-related gene comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS:1-17.

Claim 21. (Original) The method of claim 19, wherein said AMDP-related gene comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOS:2, 9, 10, 16, and 17.

Claim 22. (Original) The method of claim 19, wherein said polymorphism is within an intronic, exonic or promoter sequence of said phagocytosis-related or AMDP-related gene.

Claim 23. (Original) The method of claim 19, wherein said polymorphism is within a region of the human MT1-MMP gene that can be amplified by PCR using amplimer pairs having nucleic acid sequences selected from the group consisting of SEQ ID NOS: 18 and 19; 20 and 21; 22 and 23; 24 and 25; 26 and 27; 28 and 29; 30 and 31; 32 and 33; 34 and 35; 36 and 37; 38 and 39; 40 and 41; 42 and 43; 44 and 45; 46 and 47; 48 and 49; 50 and 51; 52 and 53; 54 and 55; 56 and 57; and 57 and 58.

Claim 24. (Original) The method of claim 19, wherein said polymorphism is within a 285 bp fragment of exon 5 of the human MT1-MMP gene.

Claim 25. (Original) The method of claim 24, wherein said polymorphism is a D273N missense polymorphism.

Claim 26. (Original) The method of claim 24, wherein said polymorphism is a P259P synonymous polymorphism.

Claim 27. (Original) A method of treating a retinal or choroidal degenerative disease or condition in a subject, the method comprising contacting a retinal or choroidal cell of said subject with a vector that includes a nucleic acid encoding an agent that down-regulates or inhibits expression of a nucleic acid or amino acid sequence of an AMDP-related or phagocytosis-related gene.

Claim 28. (Original) The method of claim 27, wherein said AMDP-related or phagocytosis-related gene is selected from the group consisting of prostaglandin D2 synthase, MT1-MMP, and AMDP-3, said genes comprising the respective nucleic acid sequences of SEQ ID NOS:2, 15 and 17.

Claim 29. (Original) The method of claim 27, wherein said agent is selected from the group consisting of a ribozyme, an antisense RNA, or an interfering RNA (RNAi) molecule.

Claim 30. (Original) A method of treating a retinal or choroidal degenerative disease or condition in a subject, the method comprising contacting a retinal or choroidal cell of said subject with a vector that includes a nucleic acid encoding a wild type or polymorphic variant of an AMDP-related or phagocytosis-related protein.

Claim 31. (Original) A composition for prevention or treatment of a retinal or choroidal degenerative disease or condition in a subject, the composition comprising an agent that blocks the expression or activity of an AMDP-related or phagocytosis-related protein.

Claim 32. (Original) The composition of claim 31, wherein said protein is MT1-MMP, prostaglandin D2 synthase or AMDP-3.

Claim 33. (Original) A composition for prevention or treatment of a retinal or choroidal degenerative disease or condition in a subject, the composition comprising a vector that includes a nucleic acid encoding a wild type or polymorphic form of an AMDP-related or phagocytosis-related protein.

Claim 34. (Original) The composition of claim 33, wherein said AMDP-related or phagocytosis-related protein is MT1-MMP.

Claim 35. (Original) A nonhuman transgenic animal comprising an isolated nucleic acid construct, said construct causing at least one cell type of said animal to overexpress MT1-MMP, prostaglandin D2 synthase or AMDP-3.

Claim 36. (Original) The transgenic animal of claim 35, wherein said overexpression is conditionally controlled.

Claim 37. (Original) The transgenic animal of claim 36, wherein said cell type is a retinal cell type selected from the group consisting of a photoreceptor, an RPE cell and a Muller cell, or a choroidal cell type selected from the group consisting of an endothelial cell, a smooth muscle cell, a leukocyte, a macrophage, a melanocyte, and a fibroblast.

Claim 38. (Original) A nonhuman transgenic animal comprising an isolated nucleic acid construct, said construct causing at least one cell type of said animal to express a polymorphic variant of an AMDP-related or phagocytosis-related nucleic acid and/or protein.

Claim 39. (Original) The transgenic animal of claim 38, wherein said polymorphic variant is correlated with an increased incidence in a population of humans with AMD, compared to a normal control population.

Claim 40. (Original) A nonhuman polytransgenic animal comprising at least a first isolated nucleic acid construct and at least a second isolated nucleic acid construct, said first construct causing at least one cell type of said animal to express a first polymorphic variant of a first gene, said first variant having an increased incidence in a population of humans with AMD, compared to a normal control population; and said second nucleic acid construct causing at least one cell type of said animal to express a second polymorphic variant of a second gene, said second variant having an increased incidence in a population of humans with AMD, compared to a normal control population, or an association with RPE phagocytosis.

Claim 41. (Original) The polytransgenic animal of claim 40, wherein said first gene is MT1-MMP.

Claim 42. (Original) The polytransgenic animal of claim 41, wherein said second gene is selected from the group consisting of ABCR, apolipoprotein E, C-C chemokine receptor-2, cystatin C, hemicentin/FIBL-6, manganese superoxide dismutase, C-C chemokine ligand/monocyte chemoattractant protein 1, and paraoxonase.

Claim 43. (Original) The polytransgenic animal of claim 41, wherein said second gene is associated with RPE phagocytosis, and is selected from the group consisting of human unknown PHG-1, prostaglandin D2 synthase, myelin basic protein, human unknown PHG-4, human unknown PHG-5, human peanut-like 2/septin 4, coactosin-like 1, clusterin, casein kinase 1 epsilon, ferritin heavy polypeptide 1, metargidin, human unknown PHG-13, retinaldehyde binding protein 1, actin gamma 1, SWI/SNF related/OSA-1 nuclear protein, and human unknown AMDP-3.

Claim 44. (Currently Amended) The transgenic animal of claim 35 ~~35, 38 or 40~~ wherein said animal is a mouse.

Claim 45. (Original) An isolated nucleic acid encoding a phagocytosis-related protein, said nucleic acid comprising SEQ ID NO:1.

Claim 46. (Original) An isolated nucleic acid encoding a phagocytosis-related protein, said nucleic acid comprising SEQ ID NO:4.

Claim 47. (Original) An isolated nucleic acid encoding a phagocytosis-related protein, said nucleic acid comprising SEQ ID NO:5.

Claim 48. (Original) An isolated nucleic acid encoding a phagocytosis-related protein, said nucleic acid comprising SEQ ID NO:12.

Claim 49. (Original) An isolated nucleic acid encoding a phagocytosis-related protein, said nucleic acid comprising SEQ ID NO:17.

Claim 50. (Original) A gene array comprising a plurality of isolated oligonucleotide sequences, said sequences being positioned within an intronic, exonic or promoter sequence of a native human AMD-related or phagocytosis-related gene sequence, wherein the genes represented in said array by said oligonucleotide sequences encode cDNAs comprising the nucleic acid sequences of SEQ ID NOS:1-17 and SEQ ID NOS:62-69.

Claim 51. (Original) The gene array of claim 50, wherein at least one gene is MT1-MMP and said oligonucleotide sequence comprises a P259P or a D273N polymorphic variant of the MT1-MMP gene sequence.

Claim 52. (Original) The gene array of claim 51, further comprising at least one oligonucleotide sequence comprising at least one polymorphic variant of an AMD-related gene selected from the group consisting of ABCR (D217N; G1961E), manganese superoxide dismutase (V47A), apolipoprotein E (C130, R176C and C130R, R176), cystatin C (A25T) and paraoxonase (Q192R, L54M).